Diabetic macular edema (DME) is the leading cause of visual loss in diabetic patients.

Currently, intravitreal anti-VEGF injections (IVIs) are considered to be the first-line therapy for treatment of DME.
Not sufficient in all cases.

*Multifactorial pathogenesis*

• One of these factors is ....

*the state of vitreoretinal interface*
OCT allows evaluation of the vitreoretinal interface (VRI) changes and allows for a pathogenesis-oriented approach possible for DME therapy.
VMA/VMT and DME

Diabetic Macular Edema (DME)
DME with ERM tend to respond poorly

DME patients with (+)VMA responded better to anti-VEGF than those (-)VMA (Sadiq et al)

VMA/VMT and Neovascular AMD

VMA or VMT can decrease the effectiveness of anti-VEGF treatment in patients with neovascular AMD
Macular Edema due to Retinal Vein Occlusion

Singh et al. -> found *no association* between VRI status and treatment outcomes with anti-VEGF agents for ME secondary to RVO

Which raises the question...
Does anti-VEGF injection induce PVD?
Singh,
PVD and Injections

Could the injection itself regardless of contents induce PVD?

Geck et al. (yes)...DME
Prospective study of 61 eyes receiving anti-VEGF and had concurrent VMA 15/61 eyes (24.6%) developed a PVD

Veloso et al. (no)....AMD
Cohort study of 125 eyes with neovascular AMD and VMA
All received at least 3 monthly anti-VEGF injections (avg 8.3)
7/125 (5.6%) eyes developed PVD, all of which had focal VMA

No injection!!!!!
Classification and Subclassification

1- VMA: (no change in the contour)
- **Focal** (≤ 1500 μm) or **broad** (> 1500 μm)
  Isolated or concurrent macular disease.

2- VMT: (change in the contour)
- **Focal** (≤ 1500 μm) or **broad** (> 1500 μm)
  Isolated or concurrent macular disease
FOCAL VMT     BROAD VMT

VM INTERFACE Abnormalities in DME

Vitreomacular interface disease has been reported to occur in up to **7% to 16%** of eyes with DME.

These anomalies include Vitreomacular Traction (VMT), Epiretinal Membrane (ERM), and Vitreomacular Adhesion (VMA). *(Chang CK, et al; 2012)*
VMA and DME

In contrast to DME without VMA:

in these conditions, an increase of retinal thickness is caused not only by upregulation of VEGF and vascular hyperpermeability, but also by anteroposterior or tangential tractions which are followed by secondary vascular hyperpermeability and retinal thickening.

D.AHMED ABD ALIM MOHAMED

DME with normal VRI
DME with ECCENTRIC ERM

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DME with CENTRAL ERM

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Effect of Vitreomacular Adhesion on Treatment Outcomes in the Ranibizumab for Edema of the Macula in Diabetes

(Sadig MA; et al 2016)
**READ-3 study**

IT is a retrospective cohort study, published in *Ophthalmology in 2016*, evaluated 26 patients with DME who had VMA and 98 patients with DME who did not have VMA.

Patients were randomized to receive monthly injections of either 0.5 mg of Lucentis for 6 months.

**At the 6-month follow-up,**

BCVA increased by a mean of 11.31 ± 6.67 letters in the group with VMA and 6.86 ± 7.58 letters in the group without VMA. Both increases were significant compared with baseline (P < .05), and the difference between the two groups was significant (P = .007).
CONCLUSIONS:

DME patients with VMA have a greater potential for improvement in visual outcomes with anti-VEGF.

Therefore, the presence of VMA should not preclude patients with DME from receiving treatment. (Sadig MA; et al 2016).

The authors attributed the higher visual gains in the group with VMA to an increased concentration of growth factors in the pre-macular hyaloid secondary to increased enzyme mediated collagen cross-linking in the vitreous.

“PVD in these eyes may lead to:

1-Remove this reservoir of growth factor from the vicinity of the retina and therefore lead to improved outcomes,”.

2-Improved transvitreal oxygenation in these patients after vitreous detachment that may lead to improvement in visual acuity.”

D.AHMED ABD ALIM MOHAMED
Vitreoretinal interface abnormalities in diabetic macular edema and effectiveness of anti-VEGF therapy: an optical coherence tomography study

Purpose: To study vitreoretinal interface (VRI) abnormalities in diabetic macular edema (DME) and the influence of these on the effectiveness of intravitreal anti-vascular endothelial growth factor (VEGF) therapy.

Methods: VRI status and central retinal thickness (CRT) were evaluated using line and 3D-reference scans obtained using spectral-domain-optical coherence tomography RTVue-100 before and 1 month after intravitreal anti-VEGF injection (IVT). VRI status was categorized into five subgroups: normal VRI, retinal surface wrinkling associated with the eccentric epiretinal membrane (ERM), ERM involving the macular center, vitreomacular adhesion (VMA), and vitreomacular traction (VMT).

Results: A total of 105 eyes of 89 patients were included in the study. One month after IVT, the mean change of CRT in normal VRI eyes and eyes with VRI abnormalities was $-128.0\pm144.7\ \mu m$ and $-53.0\pm46.4\ \mu m$ (p<0.05), respectively. The mean change of CRT 1 month after IVT in each subgroup with VRI abnormalities, apart from the subgroup with retinal wrinkling associated with eccentric ERM, was statistically significantly lower compared to the eyes with normal VRI (p<0.05).

Conclusion: VRI abnormalities significantly reduce the effectiveness of intravitreal anti-VEGF therapy in eyes with DME. Eyes with noticeable changes of VRI, including ERM involving the macular center, VMA, and VMT, have a poorer response to anti-VEGF therapy compared to eyes with normal VRI or eccentric ERM.

Keywords: diabetic macular edema, anti-VEGF, optical coherence tomography, epiretinal membrane, vitreomacular adhesion, vitreomacular traction.
LIMITATION: only **one month** follow up

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**VMA associated with poor outcomes in anti-VEGF-treated patients**

**Cheryl Guttman Krader**, Jul 20, 2017

The study included 195 eyes treated since 2012

The presence of vitreomacular adhesion (VMA) is associated with poorer, short-term anatomic, and functional outcomes in eyes with diabetic macular edema (DME) receiving anti-VEGF therapy (**Márcio B. Nehemy**)

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Mean BCVA:  
the mean BCVA at 1 month was better in the VMA-negative group than in the VMA-positive group.

Central retinal thickness:  
the magnitude of improvement was greater in VMA-negative eyes.

In the eye that presented VMA release after six injections had a better anatomic and visual outcome.

LIMITATION: only one month follow up
Benefits of Anti-Vascular Endothelial Growth Factor Therapy for Diabetic Macular Edema with and without Vitreomacular Adhesions

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Abstract

Purpose: We aimed to evaluate the effect of vitreomacular adhesion (VMA) on visual and anatomic outcomes in patients with diabetic macular edema (DME) after intravitreal injection of ranibizumab (Lucentis®). Patients and Methods: This was a prospective cohort study that included thirty eyes of DME patients, divided into two groups according to their spectral-domain optical coherence tomography imaging analysis at the baseline visit to identify the presence (VMA+) or absence (VMA−) of VMA. Patients with any degree of vitreomacular traction were not included in this study. VMA was classified by the size of adhesion into either focal (<1500 μm) or broad (<1500 μm). All patients received monthly 0.5 mg of intravitreal ranibizumab injection for 6 months. Patients were observed monthly for a 6-month period and their best-corrected visual acuity (BCVA) and central macular thickness (CMT) were recorded. The incidence of posterior vitreous detachment (PVD) was observed. Results: Compared with baseline, there was a significant decrease in CMT after 6 months by 151.46 ± 121.47 and 139.33 ± 144.29 μm in VMA+ and VMA− groups, respectively (P = 0.001). The mean average improvement in BCVA was 10.21 ± 6.33 and 6.68 ± 6.33 letters in the VMA+ and VMA− groups, respectively. The difference between the two groups was statistically significant (P = 0.007). At 6 months, among the 15 eyes of VMA+ at baseline, 4 eyes demonstrated PVD and 11 eyes showed no change in VMA status. Conclusions: Patients having DME with VMA may achieve higher visual gain with anti-vascular endothelial growth factor therapy. Presence of VMA should not preclude patients with DME from receiving anti-vascular endothelial growth factor therapy.

Keywords: Anti-vascular endothelial growth factor, diabetic macular edema, vitreomacular adhesion
Vitreomacular adhesion status change after 6 month in VMA+ group.

Focal versus broad VMA changes after 6 month.

<table>
<thead>
<tr>
<th>VMA+ (n=15)</th>
<th>Focal VMA</th>
<th>Broad VMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BCVA change from baseline To month 6 (letters)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>11.40±2.85</td>
<td>12.35±6.26</td>
</tr>
<tr>
<td>P value</td>
<td>0.82</td>
<td>0.62</td>
</tr>
<tr>
<td>Mean CMT change from baseline To month 6 (μm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ±SD</td>
<td>300.000±132.82</td>
<td>154.89±112.45</td>
</tr>
<tr>
<td>P value</td>
<td>0.02</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Of the four patients in which PVD developed:
2 patients demonstrated PVD after the first injection
one patient demonstrated PVD after five injections.
and one patient demonstrated PVD after six injections.

Baseline

CST: 449 μm
(20/50)

M6

CST: 269 μm
(20/30)
Sum of the studies

-Studies in in which the presence of VMA has better outcome had a long follow up (6 months)

While, studies in which the presence of VMA has poor outcome had a short follow up (one month)

Home message

So, we recommend to extend the number of injection in patient with DME with VMA to 6 initial injections instead of 3 or 4 injections for a better outcome and higher incidence of post injection PVD
الحمد لله رب العالمين

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